Examiner McGarry also indicated that claims drawn to variants in accordance with Example 14 of the USPTO Written Description Guidelines, if supported in the present specification, would likewise receive favorable consideration.

Claims 37-50 currently stand rejected under 35 U.S.C. §112, first paragraph based on alleged lack of written description and inadequate enablement.

In accordance with the Examiner's helpful suggestions, claim 37 has been amended to recite a pesticidal composition comprising a proteinaceous material encoded by SEQ ID NO:1. Further, new claims 59-70 have been added, which are drawn to variants of SEQ ID NO:1, drafted in accordance with Example 14 of the USPTO Written Description Guidelines.

Support for the amendment to claim 37 can be found in original claim 41, and throughout the specification, for example at page 2, lines 29-34 and page 16, lines 18-26. Support for new claims 59-70 can be found in the original claims, and throughout the specification, in particular at page 3, lines 25-29. As the present claim amendment is clearly supported by applicants' original specification, this amendment does not constitute new matter.

For the reasons set forth below, the grounds of rejection maintained in the August 12, 2002 Official Action are again respectfully traversed.

THE PRESENT CLAIMS MEET THE WRITTEN DESCRIPTION REQUIREMENT OF 35 U.S.C. §112 FIRST PARAGRAPH

Claims 37-38, 40, and 42-50 are now drawn to a composition comprising an agent encoded by the polynucleotide shown in Figure 2. New claims 59-70 are drawn to compositions comprising variants which are 90% homologous to the proteinaceous material encoded in SEQ ID No. 1, and have been drafted in accordance with the USPTO Written Description Guidelines, in particular, Example 14. Both sets of claims require that the agent have toxic activity.

The rejection is based on alleged lack of written description. As the Examiner aptly points out at the top of page 7 of the August 12, 2002 Official Action, the adequacy of the written description provided in a given specification must be determined on the merits of each case. Thus, the cited passages from cases such as University of California v. Eli Lilly & Company and Fiers v. Revel, arising out of entirely different factual contexts, are of little, if any, pertinence to the present case. It has long been held that the relevant inquiry in determining compliance with the written description requirement of 35 U.S.C. §112, first paragraph, is whether the originally filed specification reasonably conveys to a person having ordinary skill in the art that, as of the filing date of the application, applicants had possession of the claimed subject matter. In re Kaslow, 218 U.S.P.Q. 1089 (Fed. Cir. 1983).

In the present case, it is clear from applicants' specification that this inquiry must be answered in the

affirmative. The present specification clearly conveys to a person of ordinary skill in the art that, as of the filing date of this application, applicants were in possession of a pesticidal composition comprising a proteinaceous material obtainable from a *Xenorhabdus nematophilus* species encoded by the nucleotide sequence of Figure 2 and that has toxic activity when administered orally to an insect.

Furthermore, the written description guidelines set forth in the Federal Register Vol. 66, No. 4, January 5, 2001 state that "An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics, so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention."(page 1105, column 3). "An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that the applicant was in possession of the claimed invention, i.e.: complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of characteristics." (Page 1106, column 1).

Applicants' specification provides a specific structure, i.e., the polynucleotide sequence that involved the active agent of this composition, and further correlate a function (toxic activity to insects) to the structure, and thus

meet the USPTO Written Description Guidelines described above.

Whether or not applicants provided sequence information identifying the specific protein or protein variant, or established that the pesticidal activity is attributable to one or two or more proteins is inconsequential to satisfying the written description requirement. Applicants provided other information indicating their possession of the claimed invention that clearly satisfies the written description requirement. Applicants have not merely identified the organism responsible for producing the observed pesticidal activity, but also have:

A. Provided a reference sequence encoding a toxin having demonstrated oral activity (Seq ID No 1 from clone 1 of NCIMB 40887 - see Examples 7 to 9);

B. Most importantly, demonstrated that the toxicity may be transferred to other organisms by genetic engineering, through use of Seq ID No 1, and still retain the unexpected oral toxicity (see Examples 7 to 9);

C. Further demonstrated that other *Xenorhabdus* sources contain closely related sequences which are identified using hybridization (note the 11.4 kb and 9 kb fragments of NCIMB 40886 and ATCC 19061 discussed of in Example 11); and

D. Also identified effective techniques which the skilled person could use should they wish to dissect out fragments of Seq ID No 1 which retained pesticidal activity (page 8, first two paragraphs). As urged in the applicants' response to the November 20, 2001 Official Action, later authors,

including some of the present inventors, used precisely the techniques disclosed at page 8 of this specification, i.e. transposon mutagenesis, as taught by Siefert et al (1986) to identify sub-regions showing particular activity, as shown in Morgan et al. (2001) Applied & Environmental Microbiology p 2062-2069.

Although the present specification does not disclose using the bacteriophage P_L promoter to detect activity of the xptA1 protein as noted by the Examiner, the specification does disclose the use of the T7 and T3 promoters to detect the activity of the xptA1 protein. Specifically at page 22, lines 7-26, Applicants disclose that the DNA fragments were cloned into the SuperCos I vector of Startagene and transformed into *E. coli*. Supernatants from these transformed *E. coli* were tested for effects on the survival of *P. brassicae* larvae, thereby indicating the present of the insecticide. The SuperCos I vector utilizes T7 and T3 promoters for transcription of the inserted DNA. T7 and T3 promoters are functional equivalents of the P_L promoter as is well known in the art. Thus, the lack of disclosure of using a P_L promoter in the present specification is of no consequence as the use of a P_L promoter for subcloning is routine in the art.

Furthermore, at page 16, lines 18-26 of the specification, it is disclosed that various treatments affect the activity of the supernatant. The displayed properties are clearly characteristic of a proteinaceous material.

Specifically, the component of the supernatant is found to be temperature sensitive with complete loss of activity at 80° C. The temperature profile is characteristic of proteins as secondary and tertiary structures, which are critical to the proteins' function, are typically distorted or lost at these temperatures. Moreover, acetone and low levels of SDS are commonly known as protein denaturants and therefore the loss of activity in their presence is again indicative of a proteinaceous material. Conversely, Triton X-100 and nonidet P40 are known to be a mild, nonionic detergents that assist the solubilization of proteins, but are regarded as non-denaturing. The inability of these treatments to reduce the activity of the supernatant further indicates that the compound of interest is proteinaceous. Similarly, cold storage and the addition of 1M NaCl are treatments that typically do not negatively impact a protein's activity. These treatments were also determined not to effect the activity of the supernatant thereby indicating a proteinaceous compound. It would be appreciated by a skilled artisan that the combination of the results from all of the above mentioned treatments overwhelmingly point to a proteinaceous material as the agent responsible for the pesticidal activity produced by the supernatants.

Additionally, the Applicants disagree with the Examiner's position that there is not clear evidence that the toxic protein functions via the oral route. Applicants assert that because the toxin is provided to the larvae as a part of

their food source that it can be determined that the method of action is via the oral route.

Accordingly, the specification clearly demonstrates that applicant had possession of the invention as now claimed at the time of filing, and withdrawal of the rejection is respectfully requested.

THE PRESENT CLAIMS MEET THE ENABLEMENT REQUIREMENT OF 35 U.S.C. §112 FIRST PARAGRAPH

Turning to the alleged insufficiency of enablement provided by the present specification, claims 37-38, 40, and 42-50 are now drawn to a composition comprising an agent encoded by the polynucleotide shown in Figure 2. New claims 59-70 are drawn to compositions comprising proteinaceous material which is encoded by a polynucleotide which is 90% homologous to SEQ ID No. 1, and have been drafted in accordance with the USPTO Written Description Guidelines, in particular, Example 14. Both sets of claims require that the agent have toxic activity.

The Examiner's position with regard to enablement is plainly not well founded, considering that applicants have provided methods of both producing and using the claimed pesticidal agent directly from the *Xenorhabdus*, as set forth in Examples 1-6 of the specification. These examples, must be considered in conjunction with the additional data provided in applicants' specification, as noted above, showing that other *Xenorhabdus nematophilus* sources contain closely related sequences which were identified using hybridization and that

these organisms encode the same unexpected oral activity of SEQ. ID No. 1, as set forth in Examples 7-9 of the present specification. Thus, the overall disclosure of applicants' specification clearly provides enablement that is commensurate in scope with the claimed invention.

To deny applicants' patent protection to which they are clearly entitled because they have not provided specific protein sequence information or identified that the pesticidally active agent is one or two or more proteins is without adequate justification and manifestly unfair.

It will almost always be true that a given sequence (even a single gene sequence) in a patent application can be to some extent modified or truncated while still retaining some activity. However this is no justification for refusing claims based on that sequence simply because they may exclude others from using such sub-sequences. The grant of such an exclusive right is appropriate because it protects the contribution to the art of the longer sequence and its activity which will have motivated the use of any shorter sequence. This is so even if shorter sequences might themselves be patentable. This is a well established principle in patent law. Furthermore, in this connection, the Examiner should appreciate the commercial reality which is that the pesticidal agents of this invention are most likely to be practiced through genetic engineering. Protection commensurate with this contribution to the art should thus be claims encompassing genetic engineering uses of Seq ID No 1, or

sequences closely related to it or otherwise derived from it e.g. by taking the ORFS easily identified within it, so that the granted patent cannot be easily avoided by such simple expedients as a single base change, a truncated sequence, or the use of hybridizing homologues. This is the invention which the applicants made, disclosed, and which is set out in the present claims, and on which patent protection is clearly warranted.

Accordingly, in light of the amendments and arguments set forth above, withdrawal of the enablement rejection is respectfully requested.

It is noted in passing that applicants' response to the August 12, 2002 Official Action in this application included a petition for a one(1) month extension of the response period and the appropriate fee for such an extension. This submission is accompanied by a petition for an additional two (2) month extension of the response period and the required extension fee. Thus, this RCE is being filed within the three (3) month extension period.

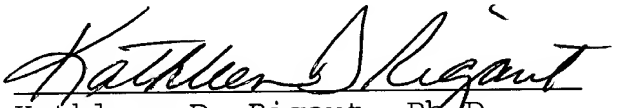
In view of the present claim amendments, and the foregoing remarks, it is respectfully urged that the rejections set forth in the August 12, 2002 Official Action be withdrawn and that this application be passed to issue, and such action is earnestly solicited.

In the event the Examiner is not persuaded as to the allowability of any of the pending claims, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number given below.

Respectfully submitted,

DANN DORFMAN HERRELL and
SKILLMAN, P.C.

Attorneys for Applicant

By 
Kathleen D. Rigaut, Ph.D.
Registration No. 43,047
For: Patrick J. Hagan
Registration No. 27,643

PJH:KDR:ksk

Marked-Up Copy of Amended Claims

37. (Twice Amended) [An isolated pesticidal agent] A pesticidal composition comprising a proteinaceous material [which is an extracellular protein] obtainable from a *Xenorhabdus nematophilus* species and which is encoded by the nucleotide sequence of Figure 2 (SEQ ID No 1)[,] [or encoded by a variant obtained from Xenorhabdus nenatophilus, the sequence of said variant hybridizing with said sequence of Figure 2 under stringent conditions,] said [protein] proteinaceous material having toxic activity when administered orally to an insect.

38. (Amended) [An agent] A composition according to claim 37, wherein the *Xenorhabdus nematophilus* species is ATCC 19061, NCIMB 40886 or NCIMB 40887.

40. (Twice Amended) [An agent] A composition according to claim 37, which

a. has oral pesticidal activity against *Pieris brassicae, Pieris rapae* and *Plutella xylostella,*

b. is substantially heat stable to 55°C,

c. acts synergistically with *B. thuringiensis* cells as an oral pesticide,

d. is substantially resistant to proteolysis by trypsin and proteinase K, and

e. has its pesticidal activity substantially destroyed by

treatment with sodium dodecyl sulphate or acetone on heating to 80°C.

42. (Amended) A composition according to claim [41] 37 which comprises a further pesticidal material not obtainable from *Xenorhabdus*.

46. (Amended) A composition according to claim [41] 37 which further comprises an agriculturally acceptable carrier.

48. (Amended) A method for killing or controlling insect pests, which method comprises administering to a pest or the environment thereof a composition according to claim [41] 37.

50. (Twice Amended) A method for killing or controlling insect pests, which method comprises administering orally to the insect a composition according to claim [41] 37.